REMARKS

This is in response to the Office Action dated March 29, 2004.

I. Status of the Claims: Claims 1-23 are pending. Claims 1-9 and 12-17 have been withdrawn from consideration. Therefore, claims 10-11 and 17-23 are currently at issue.

II. Claim Rejections: The rejections set forth by the Examiner are summarized and addressed as follows:

(a) Obviousness-Type Double Patenting: The Examiner has rejected claims 10 and 11 and new claims 17-23, under the judicially created doctrine of obviousness-type double-patenting as allegedly being unpatentable over claims 1-7 of U.S. Patent No. 6,020,143 (the "'143 patent") and/or over claims 1-6 of U.S. Patent No. 6,383,758 (the "'758 patent"). Applicants respectfully traverse the present rejection and request reconsideration in view of the following remarks.

An obviousness-type double patenting analysis requires two steps. First, the claims of the application and the claims of the prior patent must be construed. Next, a determination is made as to whether there are any differences between the claims which render the later claims patentably distinct. *Eli Lilly v. Barr Laboratories Inc.*, 251 F3d 955, 968 (Fed. Cir. 2001). The analysis is limited to the claims, as the prior patent is not prior art to the application at issue. *Panduit v. Dennison Mfg. Co.*, 774 F.2d 1082 (Fed. Cir. 1987). It is not sufficient that the prior patent may dominate a claim of a later application, rather the claim of the prior patent must render the claim of the later application obvious. If the later claim is patentably distinct, *i.e.*, non-obvious over the earlier claim of a commonly owned patent, the later claim is patentable and the provisional double patenting rejection is unwarranted. With the exception that the prior patent is not prior art to the application at issue, and that the analysis is limited to the claims, double patenting analysis parallels the inquiry for determining non-obvious under 35 U.S.C. §103. *In re Braat*, 937 F.2d 589 (Fed. Cir. 1991), *see also* MPEP §804 (8th ed., 2004).

Claim 1 of the '143 patent claims a method of identifying substances that affect the interaction of a presenilin-1-interacting protein with a mammalian presenilin-1 protein. The method of claim one comprises two steps:

(1) providing a preparation containing a mammalian presenilin-1 protein, or a fragment, variant or mutant of said mammalian presenilin-1 protein that binds to said presenilin-1-interacting protein; a presenilin-1-interacting protein; and a candidate substance; and

(2) detecting whether said candidate substance affects said interaction of said presenilin-1-interacting protein with said mammalian presenilin-1 protein, or a fragment, variant or mutant of said mammalian presenilin-1 protein that binds to said presenilin-1-interacting protein.

The method of claim 10 of the instant application claims a method for identifying a candidate compound for treating a neuropsychiatric or neurodevelopmental disorder. The method comprises two steps:

(1) contacting a reconstituted system for measuring presenilin associated membrane protein (PAMP) activity, comprising a PAMP, or a functional fragment thereof, and a PAMP substrate, with a test compound, the PAMP comprising an amino acid sequence at least 90% identical to at least one amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:16 and SEQ ID NO:18; and

(2) detecting a difference in PAMP activity in the presence of the compound compared PAMP activity in the absence of the compound, wherein a decrease in PAMP activity identifies the candidate compound.

Comparing claim 1 of the '143 patent and claim 10 of the instant application it is evident that there are differences between claim 1 of the '143 patent and claim 10 of the instant application (e.g., the use of PAMP or a functional fragment thereof, or identifying a candidate compound for treating a neurological disease) and that these differences would not have been obvious to one of ordinary skill for the following reasons:

Claim 1 of the '143 patent does not teach the use of a PAMP comprising an amino acid sequence at least 90% identical to at least one amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:16 and SEQ ID NO:18, as recited in claim 10. Claim 1

teaches the use of a *presenlin-1 binding protein*, and the '143 patent describes several presenlin-1 binding proteins, e.g., S5a subunit of the 26S proteasome, the GT24 protein and Rab11 (col. 8, ll. 6-10). The '143 patent does not teach or suggest the use of PAMP, let alone teach a specific PAMP amino acid sequence.

Not only does Claim 1 fail to specifically teach PAMP or any PAMP amino acid sequences, the claim provides no guidance or suggestion that would lead one of ordinary skill to select any one of the amino acid sequences recited in claim 10 in a method for identifying candidate compound for treating a neuropsychiatric or neurodevelopmental disorder.

Claim 1 of the '143 patent is directed to a method of identifying substances that affect the interaction of a presenilin-1-interacting protein with a mammalian presenilin-1 protein. Claim 1 does not teach that the method recited therein may be used to identifying a candidate compound for treating a neuropsychiatric or neurodevelopmental disorder as provided in the present application. The present application teaches a method of identify candidate compounds by detecting the difference in PAMP activity in the presence of a test compound (see, e.g., p. 5, ll. 3-6). The present application further teaches that alteration in PAMP activity correlates with secretion of Aβ which is associated with neuropsychiatric and/or neurodevelopmental disorder(s) (see, e.g., Example 2, p. 44, ll. 13-19). Provided the teachings of claim 1 of the '143 patent, one skilled in the art would not be motivated to modify the method of claim 1 to identifying a candidate compound for treating a neuropsychiatric or neurodevelopmental disorder, as there is no suggestion that the method of claim 1 could be modified for such a use, either in the prior art or in the claim itself.

Because there are differences between claim 1 of the '146 patent and claim 10 of the instant application and these differences would not have been obvious to one of ordinary skill, claim 10 and dependent claim 11 are patentably distinct over claim 1. Therefore claim 1 does not render obvious either claim 10 or dependent claim 11. *In re Gulack,* 703 F.2d 1381, 1385 (Fed. Cir. 1983) (For a claim to be obvious over the prior art, the prior art must teach or suggest each and every limitation of the claimed invention.) *See also* MPEP §2143.03 (8th ed., 2004).

Claims 10 and 11 are similarly non-obvious over claims 1-6 of the '758 patent. Like the claims of the '143 patent, there are differences between the claims of the '758 patent and claim 10

and these difference would not have been obvious to one of ordinary skill. Claim 1 of the '758 patent recites a two step method for identifying substances that alter the interaction of a presenilin protein with a presenilin-binding protein, comprising: the steps of:

(1) contacting at least the interacting domain of a presenilin protein to a presenilin-binding protein in the presence of a test substance, and

(2) measuring the interaction of the presenilin protein and the presenilin-binding protein.

Claim 1 of the '758 patent teaches the use of a presenilin-binding protein and the patent discloses several such proteins, e.g., S5a subunit of the 26S proteasome, Rab11, MHC and GT24 (col. 4, ll. 47-53). The '758 patent does not teach or suggest the use of PAMP let alone PAMP having any one of the amino acid sequences recited in claim 10. Furthermore, claim 1 of the '758 does not teach or suggest that the effect a compound has on PAMP activity may be used to identify a candidate compound for treating a neuropsychiatric or neurodevelopmental disorder.

The differences between the claims of the '758 patent and claim 10 would not have been obvious as there is not suggestion in the claims of the '758 that would have motivated one of ordinary skill to modify the teaching of the claims to practice the invention of claim 10. Therefore, applicants submit that the claims 10 and 11 are non-obvious over the claims of the '758 patent and respectfully request withdrawal of the present rejection.

(b) Rejections Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 10, 11 and 17 through 23 as allegedly indefinite. The Examiner maintains that: (1) it is not clear whether a decrease or increase in PAMP activity identifies the compound, (2) the term "PAMP" is unclear, and (3) it is not clear how a difference in PAMP activity correlates with a compound useful for treating a neuropsychiatric or neurodevelopmental disease.

Applicants respectfully traverse the rejection.

Applicants submit that penultimate limitation of claim 10 ("wherein the difference in PAMP activity identifies the candidate compound") is clear and unambiguous. The limitation clearly defines that a candidate compound useful in treating a neuropsychiatric or neurodevelopmental disorder may be identified by detecting a change in PAMP activity. *Any* change in PAMP activity, whether a decrease or an increase, is sufficient to identify the candidate compound.

The Examiner maintains that the term "PAMP" is unclear because the term has no structural or functional limitations. Applicants respectfully disagree with the position of the Examiner. Contrary to the Examiner's assertion, claim 10 provides both structural and function limitations on PAMP because it states "the PAMP comprising an amino acid sequence at least 90% identical to at least one amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:16 and SEQ ID NO:18." Further, the applicants have recited several sequence listings of various embodiments of PAMP as well as PAMP mutants that fall within the scope of the claimed invention (see, e.g., SEQ ID NO: 14, 16 and 18 and Example 2, page 43), Applicants have also described PAMP at great lengths in the specification, (see, e.g., page 6, line 15-page 10, line 5) and have provided several working examples which demonstrate various embodiments of the present invention which employ PAMP. Provided the recitation of specific sequence listings in the claims, extensive description of PAMP in the specification, and several working examples of PAMP, it is difficult to see how the term would be unclear to one of ordinary skill in the art.

The Examiner also maintains that it is not clear how a difference in PAMP activity correlates with a compound useful for treating a neuropsychiatric or neurodevelopmental disease. Applicants respectfully submit that the specification clearly describes the correlation between PAMP activity and neuropsychiatric or neurodevelopmental disease, and how compounds which modulate PAMP activity may be useful in treating such disease. See, e.g., page 6, line 20 through page 7, line 2, and page 42, lines 17-28. The applicants have also provided a working example, which establishes the correlation between PAMP activity (in the instant example, measured as Aβ secretion, which has been implicated in neuropsychiatric and neurodevelopmental diseases) and the modulation of the interaction between PAMP and a PAMP substrate. (Page 45, lines 18-25).

Applicants submit that the present claims are clear and unambiguous and therefore respectfully request withdrawal of the rejection, in view of the present remarks.

(c) Rejections Under 35 U.S.C. § 112, first paragraph

The Examiner has further rejected claims 10, 11 and 17 through 23 for allegedly failing meet the written description requirement. Specifically, the Examiner maintains that the specification does not describe PAMP proteins having at least 90% identity to SEQ ID NO: 14, 16 or 18 as having the recited activity. Applicants respectfully traverse the present rejection.

Applicants specifically direct the Examiner to the definition of PAMP spanning page 8, line 17 through page 9, line 12. The definition of PAMP recited in the specification embraces not only the sequence recited in claim 1, but also derivatives and variants thereof. The definition includes, but is not limited to, PAMP having conserved structural features, relative to orthologues from *D. melanogaster* and *C. elegans*, both of which are clearly PAMP orthologs or homologs but have less than 90% sequence identity to PAMP. The definition further provides for naturally occurring variants, e.g., other mammalian PAMPs, allelic variants and mutant forms.

Not only have the applicants described the claimed invention with words, they have also provided a working example of several PAMP mutants falling within the scope of claim 1. Example 2 describes the use of eight distinct PAMP mutants in an experiment to evaluate the role of PAMP in the processing of βAPP. The methods of Example 2 monitored the interaction of PAMP with a PAMP substrates and its effect on the processing of βAPP to Aβ and exemplify PAMPs having all the limitations of claim 10. (Example 2, page 43, line 20 to page 45, line 25).

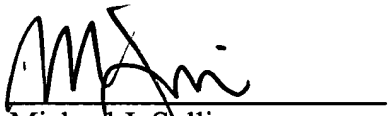
The applicants have provided both a detailed description of the invention and examples which demonstrates that the applicants were in possession of the claimed invention at the time the application was filed and therefore the present rejection is unwarranted and applicants respectfully request that it be withdrawn.

CONCLUSIONS

In view of the foregoing amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining, which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,



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